Management of HCV Treatment Failures

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The goal of anti-HCV treatment is clearance of HCV, indicated by SVR12, historically SVR24. The standard of care (SOC) for chronic hepatitis C is changing. Previously and currently still in a few of areas, Peg-IFN plus RBV is used as SOC and induce approximately 50% SVR in Caucasian, and higher in Asian. Recently approved direct-acting antiviral agents (DAAs) lead to around and higher than 90% SVR with shorter duration. However, all regimens can have treatment failure patients, regardless of Peg-IFN combining RBV, Peg-IFN combining RBV plus one DAA, and DAAs with or without RBV (interferon-free).

In chronic hepatitis C patients with genotype 1, twenty to fifty percent of patients with Peg-IFN and RBV can not achieve an SVR, which were showed as non-response, virological breakthrough, or relapse. Triple Therapy with Peg-IFN and RBV plus first-generation NS3/4A protease inhibitors still have 20% treatment failures in naive patients and 80% in previous Peg-IFN/RBV null responders. IFN-free DAAs regimens can achieve more than 90% SVR, remaining few of treatment failure are due mainly to relapse. Retreatment with Peg-IFN/RBV is never recommended due to very low SVR as lower than 5% of non-responders infected with genotype 1. In HALT-C trial, a maintenance therapy with lower dose Peg-IFN, the rates of clinical decompensation and progression were similar to untreated population, although HCV RNA were statistically reduced in the treated arm.

IFN-free DAAs regimens are very effective for treatment failure patients. Several IFN-free DAAs regimens were evaluated in genotype 1, treatment experience patients. Sofosbuvir (SOF) plus Simeprevir (SMV) induced 79%-91% SVR in experienced patients and previously non-responders, just a little lower than treatment naïve patients. In real life, 81% SVR can be observed in genotype 1 patients including first-generation PI failures, just a slightly lower than in non-failures (83%). SOF plus ledipasvir (LDV) is more effective. SVR can achieve from 87% in G1b non-cirrhotic, treatment experienced patients to 100% in both GT1a and GT1b naïve patients by combined or not RBV for 8 or 24 week, and was 95% in experienced, 98% in naïve patients by combined with or without RBV for 12 or 24 week. SOF plus daclatasvir (DCV) with or without RBV for 24 weeks was also evaluated, SVR12 achieved in 98% of the GT1 patients including protease inhibitor failures. Ombitasvir/paritaprevir boosted with ritonavir plus dasabuvir and RBV also showed 96.3% SVR for the retreatment patients who were previously treated with peginterferon-ribavirin, including 95.3% among patients with a prior relapse, 100% with a prior partial response, and 95.2% with a prior null response.

SOF/RBV was also evaluated to treat HCV genotype 2 treatment experienced patients. The SVR12 was 86% by 12 weeks and 94% with 16 weeks.

SOF/DCV 12 week regimens was also evaluated in 152 treatment-naïve and experienced GT3 patients, SVR achieved in 86% treatment experienced patients and 91% in treatment naïve patients.

A few of studies showed data on DAAs regimens failure, regimens with nonoverlapping targets or with longer treatment duration with a nucleotide inhibitor is recommended once it happen.